REMARKS

Claims 9-18 have been added, and claims 1-8 have been added. No new matter has been introduced by the instant amendments. Support for new claims 9-18 is found throughout original specification, particularly pages 110-118 and the original claims.

The Examiner has objected to claims 4, 5, 7 and 8 as being improper multiple dependent claim format. Claims 1-8 have been cancelled obviating the objection. Applicants further believe new claims 9-18 are in proper claim format.

Claims 6 and 8 are objected for failing to further limit the subject matter of a previous claim. Claims 1-8 have been cancelled obviating the objection. Applicants believe new claims 9-18 obviate multiplicity objections.

Claims 1-8 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants believe that new claims 9-18 are definite, distinctly claim the subject matter of the invention and meet the limitations of the Restriction Requirement issued on January 4, 2001.

For the sake of brevity, the prior art rejections are addressed in combination.

Claims 1-8 stand rejected under 35 U.S.C. 102(b) as being anticipated by Mahmoud et al. {Gazz. Chim. Ital., v. 112, No. 102, pp. 55-56 (1982); CA 97:72288}, Mahmoud et al. {Eur. J. Med. Chem.-Chim.Ther., v. 16, No. 4, pp. 383-384 (1981); CA 95:169076} and A. Rahman et al. {J. Indian Chem. Soc., v. 58, No. 2, pp. 171-173 (1981); CA 95:42967}.

Compounds reported in the cited documents such as Mahmoud et al '82, Mahmoud et al '81 and Rahman et al, have a N-(pyridyl)carboxamide group where the pyridyl substituent is *unsubstituted.*

Those cited compounds clearly are insufficient to sustain the instant rejection. For example, as recited by claim 1, compounds according to Formula I have a **substituted** pyridyl group as the Het group.

None of the cited references disclose or otherwise suggest such substituted compounds as Applicants claim. Accordingly, the rejection should be withdrawn. See, for instance, *In re Marshall*, 198 USPQ 344, 346 ("[r]ejections under 35 USC 102 are proper only when the claimed subject matter is identically disclosed or described in the prior art.").

Claims 1-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mahmoud et al. {Gazz. Chim. Ital., v. 112, No. 102, pp. 55-56 (1982); CA 97:72288}, Mahmoud et al. {Eur. J. Med. Chem.-Chim.Ther., v. 16, No. 4, pp. 383-384 (1981); CA 95:169076} and A. Rahman et al. {J. Indian Chem. Soc., v. 58, No. 2, pp. 171-173 (1981); CA 95:42967}; Hirai et al. {JP 04139172} and Higley et al. {U.S. Patent 5,290,801}, each taken alone.

As the Office Action is understood, the position is taken that the cited documents report benzoxazole compounds. The position is further taken that those reported compounds are related to Applicants' claimed subject matter.

The rejections is traversed.

The cited art, whether considered alone or in combination, neither teach nor suggest Applicants' compounds of Formula I, pharmaceutical compositions comprising same or therapeutic methods using compounds of Formula I.

The deficiencies of Mahmoud et al '82, Mahmoud et al '81 and Rahman et al have been discussed above, i.e., those documents report certain compounds having an *unsubstituted* pyridyl group.

Hirai et al recites certain alpha-sulfinyl-substituted acetamide derivatives.

Those compounds clearly do not render Applicants' claimed subject matter obvious. Among other things, Hirai neither discloses nor suggests that compounds of the instant invention having an alkylene linker with more than one carbon between the Y and Z group and/or having a substituted pyridyl group would be desirable or possess desirable anti-ulcer activity.

Indeed, Applicants' compounds provide for a substituted pyridyl where Hirai calls for unsubstituted pyridyl. Applicants' compounds also provide for a $(CH_2)_n$ alkylene linking group having n between 2 and 15 inclusive where Hirai calls for a methylene linker.

Such structural distinction makes clear that a *prima facie* case of obviousness is not presented by Hirai. Much greater structural similarity has been required to suatain a Secton 103 rejection. For example, in *In re Grabiak*, 226 USPQ 872, the Court of Appeals for the Federal Circuit reversed a rejection under Section 103 on the basis that the prior art provided no suggestion to replace oxygen (in an ester f the prior art compound) with a sulfur (to provide the thioester of the claimed compound). The Federal Circuit particularly noted (page 872):

> The PTO cited no pertinent reference showing or suggesting to one of ordinary skill in the art the change of a thioester for an ester group. In the absence f such reference, there is inadequate support for the PTO's position that this modification would *prima facie* have been obvious.

Higley is clearly not relevant to Applicants' claimed invention. Higley et al discloses ACAT inhibitors having urea functional groups, e.g., Z is a NR groups. Higley neither discloses nor suggests that compounds having other types of functional groups other than ureas would be suitable or advantageous for use as ACAT inhibitors.

It is also clear that the cited documents are not relevant to Applicants' methods of treating hyperlipemia, arteriosclerosis, cerebrovascular accidents, ischemic heart disease, ischemic intestinal disease or aortic aneurysm, as recited in claims 15-18.

Accordingly, reconsideration and withdrawal of the rejections are thus requested.

It is believed that the application is in condition for immediate allowance, which action is earnestly solicited.

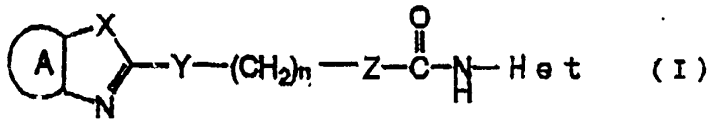
Respectfully submitted,

Peter F. Corless (Reg. No. 33860)
John B. Alexander (Reg. No.: 48399)
Dike, Bronstein, Roberts & Cushman IP Group
EDWARDS & ANGELL, LLP
P.O. Box 9169
Boston, MA 02209
Tel. (617) 439-4444

VERSION MARKED TO SHOW CHANGES

(Additions are underlined; deletions are bracketed.)

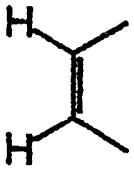
9 (new) Compounds represented by the formula (I)



(I)

wherein

represents an optionally substituted divalent residue of benzene, pyridine, cyclohexane or naphthalene, or a group:



;

Het represents a substituted pyridyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

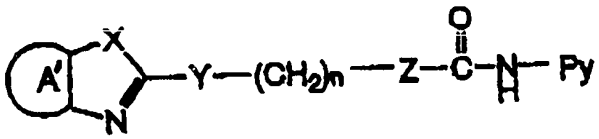
Y represents $-NR_4$ -, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15 (except that n is 1), or salts or solvates thereof.

10. (new) The compounds according to claim 9, which are represented by the formula (IA)



(I A)

wherein

represents an optionally substituted divalent residue of benzene or pyridine;

Py represents a substituted pyridyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents $-NR_4$,-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

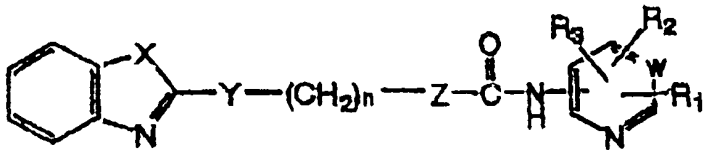
Z represents a single bond;

R_4, represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15 (except that n=1);

or salts or solvates thereof.

11. (new) The compounds according to claim 9, which are represented by the formula (III)



(III)

wherein, W represents =CH-;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents $-NR_4$-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

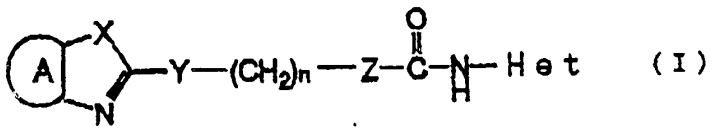
R_1, R_2, and R_3, are the same or different, and each represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a halogen atom, a hydroxyl group, a phosphate group, a

sulfonamide group, a lower alkylthio group or an optionally substituted amino group, or two of R_1, R_2, and R_3, together form an alkylenedioxide group (except that R_1, R_2 and R_3, all are a hydrogen);

R_4, represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15 (except that n is 1), or salts or solvates thereof.

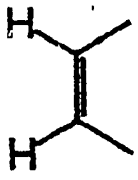
12. (new) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one compound selected from the compounds represented by the formula (I)



(I)

wherein

represents an optionally substituted divalent residue of benzene, pyridine, cyclohexane or naphthalene, or a group:



;

Het represents a substituted pyridyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents -NR,-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

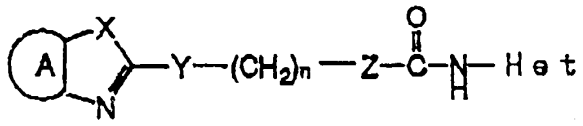
R_4, represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15 (except that n is 1), or salts or solvates thereof.

13. (new) The pharmaceutical composition according to claim 12, which is an ACAT inhibitor, an intracellular cholesterol. transfer inhibitor, a blood cholesterol depressant or a macrophage foamation suppressant.

14. (new) The pharmaceutical composition according to claim 12 or 13, which is a remedy or a medication for preventing hyperlipemia, arteriosclerosis, cerebrovascular accidents, ischemic heart disease, ischemic intestinal disease or aortic aneurysm.

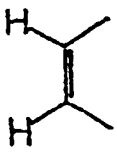
15. (new) The method for treating hyperlipemia, arteriosclerosis, cerebrovascular accidents, ischemic heart disease, ischemic intestinal disease or aortic aneurysm in need of such treatment using compounds of the formula (I')



(I')

wherein

represents an optionally substituted divalent residue of benzene, pyridine, cyclohexane or naphthalene, or a group:



;

Het represents substituted or unsubstituted pyridyl or pyrimidyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents $-NR_4$,-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

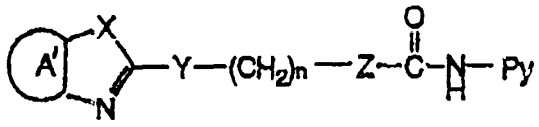
Z represents a single bond;

R_4, represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15;

or salts or solvates thereof.

16. (new) The method of claim 15 using compounds of the formula (I'A)



(I'A)

wherein

represents an optionally substituted divalent residue of benzene or pyridine;

Py represents an optionally substituted pyridyl or pyrimidyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents $-NR_4-$, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

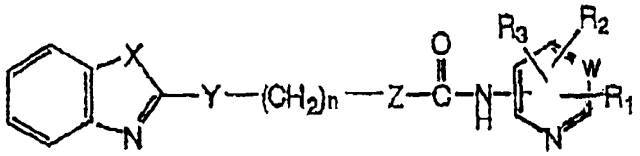
Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group;

n is an integer of from 1 to 15,

or salts or solvates thereof.

17. (new) The method of claim 15 using compounds of the formula (III')



(III')

wherein, w represents =CH- or =N-,

x represents -NH-, an oxygen atom or a sulfur atom;

Y represents $-NR_4-$ an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

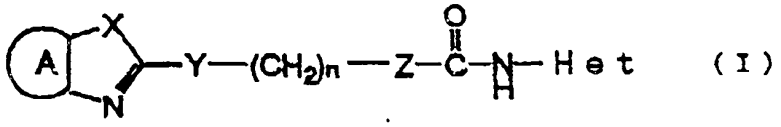
R_1 R_2, and R_3, are the same or different, and each represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a halogen atom, a hydroxyl group, a phosphate group, a sulfonamide group, a lower alkylthio group or an optionally substituted amino group, or two of R_1, R_2, and R_3, together form an alkylenedioxide group;

R_4, represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15;

or salts or solvates thereof.

18. (new) A method claim 15 using a compound represented by the formula (I), wherein



(I)

wherein

represents an optionally substituted divalent residue of benzene;

Het represents a substituted or unsubstituted pyridyl group;

X is an oxygen atom;

Y is a sulfur atom;

Z is a single bond;

n is 1;

or salts or solvates thereof.